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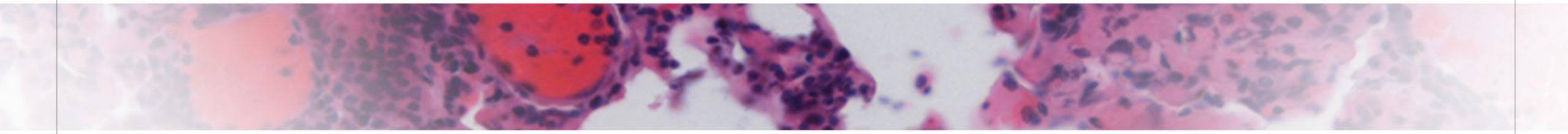

Safety and Antitumor Activity Study Evaluating Loncastuximab Tesirine and Rituximab Versus Immunochemotherapy in Diffuse Large B-Cell Lymphoma

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Introduction

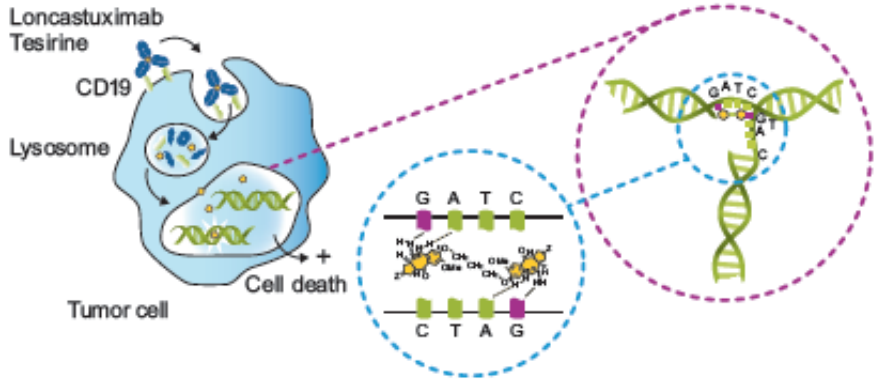
The prognosis of patients with DLBCL whose disease is refractory to initial chemotherapy (and are thus ineligible for ASCT) or relapse early after ASCT is extremely poor[1,2]

The development of a more effective, less toxic salvage treatment for DLBCL remains an unmet need[2]

Loncastuximab tesirine (Lonca) is an ADC comprising a humanized monoclonal anti-CD19 antibody conjugated to a pyrrolobenzodiazepine (PBD) dimer toxin, through a protease cleavable valine–alanine linker

Rituximab is an anti-CD20 monoclonal antibody used as a standard component of care for the treatment of DLBCL, either as monotherapy or in combination with chemotherapy

Mechanism of action of Lonca



In a Phase 2 study, Lonca demonstrated single-agent antitumor activity with manageable toxicity in patients with R/R DLBCL[3]

Rituximab is licensed for treatment of NHL but is being used in combination with an unlicensed drug (loncastuximab tesirine) in this study

1. Crump M, et al. *Blood* 2017;130:1800–8; 2. Gisselbrecht C, Van Den Neste E. *Br J Haematol* 2018;182:633–43; 3. Carlo-Stella C, et al. EHA Congress 2020. Abstract S233.

ADC, antibody-drug conjugate; **ASCT**, autologous stem cell transplantation; **DLBCL**, diffuse large B-cell lymphoma; **Lonca-R**, loncastuximab tesirine plus rituximab; **NHL**, non-Hodgkin lymphoma; **R-GemOx**, rituximab/gemcitabine/oxaliplatin; **R/R**, relapsed/refractory.

Study Design

This Phase 3, randomized, open-label, two-part, two-arm, global study of Lonca-R versus standard immunochemotherapy in patients with R/R DLBCL (NCT04384484) is currently recruiting patients

DLBCL, diffuse large B-cell lymphoma; **Lonca-R**, loncastuximab tesirine plus rituximab; **R-GemOx**, rituximab/gemcitabine/oxaliplatin; **Q2W**, every 2 weeks; **Q3W**, every 3 weeks; **R/R**, relapsed/refractory.

Study Objectives and Endpoints

Primary Objective

Evaluate the efficacy of Lonca-R versus R-GemOx

Primary Endpoint

PFS[a] (by independent central review)

Secondary Objectives

- Further efficacy evaluation
- Characterize the safety profile of Lonca-R
- Characterize the pharmacokinetics of Lonca-R
- Characterize the immunogenicity of Lonca-R
- Evaluate the impact of Lonca-R on PROs, and overall health status

Secondary Endpoints

- OS, ORR, CRR, and DoR
- Frequency and severity of AEs, and laboratory values
- Lonca PK parameters
- Anti-drug antibody titers to Lonca
- Changes in PROs from baseline

[a]Defined as time between randomization and the first documentation of recurrence or progression, or death from any cause.

AE, adverse event; **CRR**, complete response rate; **DoR**, duration of response; **Lonca-R**, loncastuximab tesirine plus rituximab; **ORR**, overall response rate; **OS**, overall survival; **PFS**, progression-free survival; **PK**, pharmacokinetics; **PRO**, patient-reported outcome;
R-GemOx, rituximab/gemcitabine/oxaliplatin.

Inclusion and Exclusion Criteria

Key Inclusion Criteria

- Adults with a pathologic diagnosis of R/R DLBCL (WHO 2016 classification), or HGBCL, with MYC and BCL2 and/or BCL6 rearrangements
- R/R disease following at least one multiagent systemic treatment regimen
- Measurable disease (2014 Lugano Classification)
- Not a candidate for SCT based on performance status, advanced age, and/or significant medical comorbidities (as considered by the investigator)
- Patients who have received previous CD19-directed therapy must have a biopsy which shows CD19 expression after completion of the CD19-directed therapy
- ECOG performance status 0–2
- Adequate organ function

Key Exclusion Criteria

- Previous treatment with Lonca or R-GemOx
- ASCT within 30 days prior to start of study drug
- Allogeneic SCT within 60 days prior to start of study drug
- Lymphoma with active CNS involvement, including leptomeningeal disease
- Serologic evidence of chronic HBV infection and unable or unwilling to receive standard prophylactic antiviral therapy or with detectable HBV viral load
- Serologic evidence of HCV infection without completion of curative treatment or with detectable HCV viral load
- Clinically significant third-space fluid accumulation (ie, ascites requiring drainage, or pleural effusion either requiring drainage or associated with shortness of breath)
- Major surgery, radiotherapy, chemotherapy or other antineoplastic therapy within 14 days prior to start of study drug, unless approved by Sponsor

ASCT, autologous stem cell transplant; **DLBCL**, diffuse large B-cell lymphoma; **HGBCL**, high-grade B-cell lymphoma; **CNS**, central nervous system; **ECOG**, Eastern Cooperative Oncology Group; **HBV**, hepatitis B virus; **HCV**, hepatitis C virus; **Lonca**, loncastuximab tesirine; **R-GemOx**, rituximab/gemcitabine/oxaliplatin; **R/R**, relapsed/refractory; **SCT**, stem cell transplant; **WHO**, World Health Organization.

Study Assessments

Efficacy

Disease assessment

- Imaging (PET-CT)[a]
- Clinical examination for lymphoma

Safety

- Adverse events
- ECOG performance status
- Hematology and chemistry
- Physical examination
- Pregnancy test (if applicable)
- Vital signs
- Weight
- 12-lead ECG

PK and Immunogenicity

- PK of Lonca PBD-conjugated Ab, total Ab, and SG3199 free warhead
- ADA in blood

Symptoms, PROs, and Overall Health

- EORTC QLQ-C30
- EQ-5D-5L
- LymS subscale of FACT-Lym
- GP5 item of FACT-Lym

[a]Performed at 6 and 12 weeks after Cycle 1, Day 1, then every 12 weeks until end-of-treatment.

Ab, antibody; **ADA**, anti-drug antibody; **ECG**, electrocardiogram; **ECOG**, Eastern Cooperative Oncology Group; **EORTC**, European Organization for Research and Treatment of Cancer; **EQ-5D-5L**, EuroQol-5 Dimensions-5 Levels; **FACT-Lym**, Functional Assessment of Cancer Therapy– Lymphoma; **Lonca**, loncastuximab tesirine; **LymS**, lymphoma subscale; **PBD**, pyrrolobenzodiazepine; **PET-CT**, positron emission tomography and computerized tomography; **PK**, pharmacokinetic; **PROs**, patient-reported outcomes; **QLQ**, Quality of Life Questionnaire.

Current Status

Recruitment

This Phase 3, randomized, open-label, two-part, two-arm study of Lonca-R versus standard immunochemotherapy in patients with R/R DLBCL (NCT04384484) is currently recruiting patients:

- Global: North America and Europe
- Target N=20 for Part 1
- Target N=350 for Parts 1 and 2 combined

DLBCL, diffuse large B-cell lymphoma; **Lonca-R**, loncastuximab tesirine plus rituximab; **R/R**, relapsed/refractory.

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